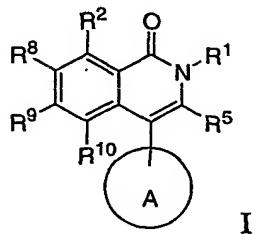


## WHAT IS CLAIMED IS:

## 1. A compound of the structure:



5 or a pharmaceutically acceptable salt, crystal form, or hydrate, wherein:  
A is

a) an aryl ring, wherein any stable aryl ring atom is independently unsubstituted or substituted  
with

- 10 1) halogen,
- 2) NO<sub>2</sub>,
- 3) CN,
- 4) CR<sup>46</sup>=C(R<sup>47</sup>R<sup>48</sup>)<sub>2</sub>,
- 5) C≡C R<sup>46</sup>,
- 6) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>OR<sup>46</sup>,
- 15 7) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>R<sup>47</sup>),
- 8) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>C(O)R<sup>46</sup>,
- 9) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>C(O)OR<sup>46</sup>,
- 10) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>R<sup>46</sup>,
- 11) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>S(O)O-2R<sup>61</sup>,
- 20 12) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>S(O)O-2N(R<sup>46</sup>R<sup>47</sup>),
- 13) OS(O)O-2R<sup>61</sup>,
- 14) N(R<sup>46</sup>)C(O)R<sup>47</sup>,
- 15) N(R<sup>46</sup>)S(O)O-2R<sup>61</sup>,
- 16) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>)R<sup>61</sup>,
- 25 17) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>)R<sup>61</sup>OR<sup>47</sup>,
- 18) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>)(CR<sup>k</sup>R<sup>l</sup>)<sub>s</sub>C(O)N(R<sup>47</sup>R<sup>48</sup>),
- 19) N(R<sup>46</sup>)(CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>R<sup>61</sup>,
- 20) N(R<sup>46</sup>)(CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>47</sup>R<sup>48</sup>),
- 21) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>C(O)N(R<sup>47</sup>R<sup>48</sup>), or

22) oxo, or

- b) a heteroaryl ring selected from the group consisting of  
5      a 5-membered unsaturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms  
selected from the group consisting of N, O or S,  
a 6-membered unsaturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms  
selected from the group consisting of N, O and S, and  
a 9- or 10-membered unsaturated bicyclic ring with 1, 2, 3 or 4 heteroatom ring atoms  
selected from the group consisting of N, O or S;

10

wherein any stable S heteroaryl ring atom is unsubstituted or mono- or di-substituted with  
oxo, and any stable C or N heteroaryl ring atom is independently unsubstituted or  
substituted with

15

- 1) halogen,
- 2) NO<sub>2</sub>,
- 3) CN,
- 4) CR<sup>46</sup>=C(R<sup>47</sup>R<sup>48</sup>)<sub>2</sub>,
- 5) C≡CR<sup>46</sup>,
- 6) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>OR<sup>46</sup>,
- 7) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>R<sup>47</sup>),
- 8) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>C(O)R<sup>46</sup>,
- 9) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>C(O)OR<sup>46</sup>,
- 10) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>R<sup>46</sup>,
- 11) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>S(O)<sub>0-2</sub>R<sup>61</sup>,
- 12) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>S(O)<sub>0-2</sub>N(R<sup>46</sup>R<sup>47</sup>),
- 13) OS(O)<sub>0-2</sub>R<sup>61</sup>,
- 14) N(R<sup>46</sup>)C(O)R<sup>47</sup>,
- 15) N(R<sup>46</sup>)S(O)<sub>0-2</sub>R<sup>61</sup>,
- 16) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>)R<sup>61</sup>,
- 17) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>)R<sup>61</sup>OR<sup>47</sup>,
- 18) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>46</sup>)(CR<sup>k</sup>R<sup>l</sup>)<sub>s</sub>C(O)N(R<sup>47</sup>R<sup>48</sup>),
- 19) N(R<sup>46</sup>)(CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>R<sup>61</sup>,
- 20) N(R<sup>46</sup>)(CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>N(R<sup>47</sup>R<sup>48</sup>),
- 21) (CR<sup>i</sup>R<sup>j</sup>)<sub>r</sub>C(O)N(R<sup>47</sup>R<sup>48</sup>), or
- 35      22) oxo;

R<sup>1</sup> is selected from the group consisting of

- 1) hydrogen,
- 2) (C<sup>a</sup>R<sup>b</sup>)<sub>n</sub>R<sup>40</sup>
- 3) (C<sup>a</sup>R<sup>b</sup>)<sub>n</sub>OR<sup>40</sup>,
- 5) (C<sup>a</sup>R<sup>b</sup>)<sub>n</sub>N(R<sup>40</sup>R<sup>41</sup>),
- 5) (C<sup>a</sup>R<sup>b</sup>)<sub>n</sub>N(R<sup>40</sup>)C(O)OR<sup>41</sup>,
- 6) (C<sup>a</sup>R<sup>b</sup>)<sub>n</sub>N(R<sup>40</sup>)(CR<sup>c</sup>R<sup>d</sup>)<sub>2</sub>N(R<sup>41</sup>)C(O)R<sup>49</sup>,
- 7) C<sub>3-8</sub> cycloalkyl,
- 8) (C<sup>a</sup>R<sup>b</sup>)<sub>n</sub>C(O)OR<sup>40</sup>,
- 10) (C<sup>a</sup>R<sup>b</sup>)<sub>n</sub>N(R<sup>40</sup>)(CR<sup>c</sup>R<sup>d</sup>)<sub>1-3</sub>R<sup>41</sup>,
- 10) (C<sup>a</sup>R<sup>b</sup>)<sub>n</sub>S(O)O-2R<sup>6</sup>,
- 11) (C<sup>a</sup>R<sup>b</sup>)<sub>n</sub>S(O)O-2N(R<sup>40</sup>R<sup>41</sup>),
- 12) (C<sup>a</sup>R<sup>b</sup>)<sub>n</sub>N(R<sup>40</sup>)R<sup>6</sup>OR<sup>41</sup>,
- 13) (C<sup>a</sup>R<sup>b</sup>)<sub>n</sub>N(R<sup>40</sup>)(CR<sup>c</sup>R<sup>d</sup>)O-6C(O)N(R<sup>41</sup>R<sup>42</sup>);

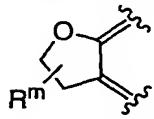
15 R<sup>5</sup> is selected from the group consisting of

- 1) C(O)N(R<sup>55</sup>R<sup>50</sup>),
- 2) C(O)OR<sup>55</sup>, and
- 3) C(O)R<sup>82</sup>;

R<sup>2</sup>, R<sup>8</sup>, R<sup>9</sup> and R<sup>10</sup> are independently selected from:

- 20 1) hydrogen,
- 2) halogen,
- 3) NO<sub>2</sub>,
- 4) CN,
- 5) CR<sup>43</sup>=C(R<sup>44</sup>R<sup>45</sup>),
- 25 6) C≡CR<sup>43</sup>,
- 7) (CRE<sup>f</sup>)<sub>p</sub>OR<sup>43</sup>,
- 8) (CRE<sup>f</sup>)<sub>p</sub>N(R<sup>43</sup>R<sup>44</sup>),
- 9) (CRE<sup>f</sup>)<sub>p</sub>C(O)R<sup>43</sup>,
- 10) (CRE<sup>f</sup>)<sub>p</sub>C(O)OR<sup>43</sup>,
- 30 11) (CRE<sup>f</sup>)<sub>p</sub>R<sup>43</sup>,
- 12) (CRE<sup>f</sup>)<sub>p</sub>S(O)O-2R<sup>60</sup>,
- 13) (CRE<sup>f</sup>)<sub>p</sub>S(O)O-2N(R<sup>43</sup>R<sup>44</sup>),
- 14) OS(O)O-2R<sup>60</sup>,
- 15) N(R<sup>43</sup>)C(O)R<sup>44</sup>,

- 16)  $N(R^{43})S(O)O-2R^{60}$ ,  
 17)  $(CREf)_pN(R^{43})R^{60}$ ,  
 18)  $(CREf)_pN(R^{43})R^{60}OR^{44}$ ,  
 19)  $(CREf)_pN(R^{43})(CRgRh)_qC(O)N(R^{44}R^{45})$ ,  
 5      20)  $N(R^{43})(CREf)_pR^{60}$ ,  
 21)  $N(R^{43})(CREf)_pN(R^{44}R^{45})$ , and  
 22)  $(CREf)_pC(O)N(R^{43}R^{44})$ ,  
 or  $R^2$  and  $R^8$  are independently as defined above, and  $R^9$  and  $R^{10}$ , together with  
 the atoms to which they are attached, form the ring



10      , where  $R^m$  is C<sub>1</sub>-6alkyl;

$R^a, R^b, R^c, R^d, R^e, R^f, R^g, R^h, R^i, R^j, R^k$  and  $R^l$  are independently selected from the group  
 consisting of:

- 15      1) hydrogen,  
 2) C<sub>1</sub>-C<sub>6</sub> alkyl,  
 3) halogen,  
 4) aryl,  
 5)  $R^{80}$ ,  
 6) C<sub>3</sub>-C<sub>10</sub> cycloalkyl, and  
 7) OR<sup>4</sup>,

20      said alkyl, aryl, and cycloalkyl being unsubstituted, monosubstituted with  $R^7$ ,  
 disubstituted with  $R^7$  and  $R^{15}$ , trisubstituted with  $R^7$ ,  $R^{15}$  and  $R^{16}$ , or  
 tetrasubstituted with  $R^7$ ,  $R^{15}$ ,  $R^{16}$  and  $R^{17}$ ;

25       $R^4, R^{40}, R^{41}, R^{42}, R^{43}, R^{44}, R^{45}, R^{46}, R^{47}, R^{48}, R^{49}, R^{50}, R^{51}, R^{52}$ , and  $R^{55}$  are  
 independently selected from the group consisting of

- 30      1) hydrogen,  
 2) C<sub>1</sub>-C<sub>6</sub> alkyl,  
 3) C<sub>3</sub>-C<sub>10</sub> cycloalkyl,  
 4) aryl,  
 5)  $R^{81}$ ,  
 6) CF<sub>3</sub>,  
 7) C<sub>2</sub>-C<sub>6</sub> alkenyl, and  
 8) C<sub>2</sub>-C<sub>6</sub> alkynyl,

said alkyl, aryl, and cycloalkyl is unsubstituted, mono-substituted with R<sup>18</sup>, di-substituted with R<sup>18</sup> and R<sup>19</sup>, tri-substituted with R<sup>18</sup>, R<sup>19</sup> and R<sup>20</sup>, or tetra-substituted with R<sup>18</sup>, R<sup>19</sup>, R<sup>20</sup> and R<sup>21</sup>;

5 R<sup>6</sup>, R<sup>60</sup>, R<sup>61</sup>, and R<sup>62</sup> are independently selected from the group consisting of

- 1) C<sub>1</sub>-C<sub>6</sub> alkyl,
- 2) aryl,
- 3) R<sup>83</sup>, and
- 4) C<sub>3</sub>-C<sub>10</sub> cycloalkyl;

10 said alkyl, aryl, and cycloalkyl is unsubstituted, mono-substituted with R<sup>26</sup>, di-substituted with R<sup>26</sup> and R<sup>27</sup>, tri-substituted with R<sup>26</sup>, R<sup>27</sup> and R<sup>28</sup>, or tetra-substituted with R<sup>26</sup>, R<sup>27</sup>, R<sup>28</sup> and R<sup>29</sup>;

R<sup>7</sup>, R<sup>15</sup>, R<sup>16</sup>, R<sup>17</sup>, R<sup>18</sup>, R<sup>19</sup>, R<sup>20</sup>, R<sup>21</sup>, R<sup>26</sup>, R<sup>27</sup>, R<sup>28</sup>, and R<sup>29</sup> are independently selected from the group consisting of

15 1) C<sub>1</sub>-C<sub>6</sub> alkyl,

- 2) halogen,
- 3) OR<sup>51</sup>,
- 4) CF<sub>3</sub>,

5) aryl,

20 6) C<sub>3</sub>-C<sub>10</sub> cycloalkyl,

7) R<sup>84</sup>,

8) S(O)<sub>0-2</sub>N(R<sup>51</sup>R<sup>52</sup>),

9) C(O)OR<sup>51</sup>,

10) C(O)R<sup>51</sup>,

25 11) CN,

12) C(O)N(R<sup>51</sup>R<sup>52</sup>),

13) N(R<sup>51</sup>)C(O)R<sup>52</sup>,

14) S(O)<sub>0-2</sub>R<sup>62</sup>,

15) NO<sub>2</sub>, and

30 16) N(R<sup>51</sup>R<sup>52</sup>);

R<sup>80</sup>, R<sup>81</sup>, R<sup>82</sup>, R<sup>83</sup>, and R<sup>84</sup> are independently selected from a group of unsubstituted or substituted heterocyclic rings consisting of a 4-6 membered unsaturated or saturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting N, O and S, and a

9- or 10-membered unsaturated or saturated bicyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting of N, O or S; and

n, p, q, r, and s are independently 0, 1, 2, 3, 4, 5 or 6.

5           2.       A compound of Claim 1, or a pharmaceutically acceptable salt thereof, wherein

A is an aryl ring selected from phenyl, unsubstituted or substituted as in Claim 1, or a heteroaryl ring, unsubstituted or substituted as in Claim 1, selected from the group consisting of pyridine, pyrimidine, pyrazine, pyridazine, indole, pyrrolopyridine, benzimidazole, benzoxazole,

10          benzothiazole, and benzoxadiazole;

R<sup>2</sup>, R<sup>8</sup>, R<sup>9</sup> and R<sup>10</sup> are independently selected from the group consisting of:

- 1) hydrogen,
- 2) halogen,
- 3) OR<sup>43</sup>, and
- 4) (CRERF)<sub>p</sub>R<sup>43</sup>,

15          or R<sup>2</sup> and R<sup>8</sup> are independently as defined above, and R<sup>9</sup> and R<sup>10</sup>, together with the atoms to which they are attached, form the ring



R<sup>1</sup> is selected from the group consisting of

- 20       1) hydrogen,
- 2) (CRAb)<sub>1-2</sub>R<sup>40</sup>
- 3) (CRAb)<sub>1-2</sub>OR<sup>40</sup>,
- 4) (CRAb)<sub>1-2</sub>N(R<sup>40</sup>R<sup>41</sup>),
- 5) (CRAb)<sub>1-2</sub>N(R<sup>40</sup>)C(O)OR<sup>41</sup>,
- 25       6) (CRAb)<sub>1-2</sub>N(R<sup>40</sup>)(CRCRd)<sub>2</sub>N(R<sup>41</sup>)C(O)R<sup>49</sup>,
- 7) (CRAb)<sub>1-2</sub>C(O)OR<sup>40</sup>,
- 8) (CRAb)<sub>1-2</sub>N(R<sup>40</sup>)(CRCRd)<sub>1-3</sub>R<sup>41</sup>, and
- 9) cyclopropyl.

30           3.       A compound of Claim 2, or a pharmaceutically acceptable salt thereof, wherein

R<sub>2</sub>, R<sub>8</sub>, R<sub>9</sub> and R<sub>10</sub> are independently selected from the group consisting of

- 1) hydrogen,
- 2) halogen, and
- 3) (C<sub>RE</sub>R<sub>f</sub>)<sub>p</sub>OR<sub>43</sub>.

5

4. A compound of Claim 3, or a pharmaceutically acceptable salt thereof,  
wherein

R<sub>1</sub> is selected from the group consisting of

- 1) hydrogen,
- 2) (C<sub>RA</sub>R<sub>b</sub>)<sub>n</sub>R<sub>40</sub>, and
- 3) (C<sub>RA</sub>R<sub>b</sub>)<sub>n</sub>OR<sub>40</sub>.

10

5. A compound of Claim 4, or a pharmaceutically acceptable salt thereof,  
wherein

15 A is an aryl ring, wherein the aryl ring atom is unsubstituted or substituted with halogen; and

R<sub>5</sub> is selected from the group consisting of

- 1) C(O)N(R<sub>55</sub>R<sub>50</sub>),
- 2) C(O)OR<sub>55</sub>, and
- 3) C(O)R<sub>82</sub>.

20

6. A compound of Claim 5, or a pharmaceutically acceptable salt thereof,  
wherein

R<sub>1</sub> is -CH<sub>3</sub>, -CH<sub>2</sub>CHCH<sub>2</sub>, or cyclopropyl;

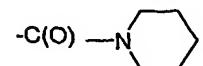
R<sub>2</sub> and R<sub>10</sub> are hydrogen;

25 R<sub>8</sub> is hydrogen or -OCH<sub>3</sub>;

R<sub>9</sub> is hydrogen or -OCH<sub>3</sub>; and

R<sub>5</sub> is selected from the group consisting of

-C(O)N(CH<sub>3</sub>)<sub>2</sub>, -C(O)NH<sub>2</sub>, -C(O)OCH<sub>3</sub>, -C(O)OH, -C(O)OCH<sub>2</sub>CH<sub>3</sub>, and



30

7. A compound of Claim 6, or a pharmaceutically acceptable salt thereof, selected from the group consisting of

4-(3-fluorophenyl)-6-methoxy-n,n,2-trimethyl-1-oxo-1,2-dihydroisoquinoline-3-carboxamide,

4-(3-fluorophenyl)-6-methoxy-2-methyl-3-(pyrrolidin-1-ylcarbonyl)isoquinolin-1(2H)-one,

2-allyl-6-methoxy-1-oxo-4-phenyl-1,2-dihydroisoquinoline-3-carboxamide,

6-methoxy-2-methyl-4-phenyl-3-pyridin-2-ylisoquinolin-1(2h)-one,

2-cyclopropyl-6-methoxy-4-phenyl-3-(1,3-thiazol-2-yl)isoquinolin-1(2h)-one,

methyl 4-(3-fluorophenyl)-6-methoxy-2-methyl-1-oxo-1,2-dihydroisoquinoline-3-carboxylate,

methyl 6-methoxy-2-methyl-1-oxo-4-phenyl-1,2-dihydroisoquinoline-3-carboxylate,

7-methoxy-2-methyl-1-oxo-4-phenyl-1,2-dihydroisoquinoline-3-carboxylic acid,

methyl 7-methoxy-2-methyl-1-oxo-4-phenyl-1,2-dihydroisoquinoline-3-carboxylate, and

ethyl 2-methyl-1-oxo-4-phenyl-1,2-dihydroisoquinoline-3-carboxylate.

5 8. A method of treating a condition in a mammal, the treatment of which is effected or facilitated by Kv1.5 inhibition, which comprises administering a compound of Claim 1 in an amount that is effective at inhibiting Kv1.5.

9. A method of Claim 8, wherein the condition is cardiac arrhythmia.

10 10. A method of Claim 9, wherein the cardiac arrhythmia is atrial fibrillation.

11. A method of Claim 9, wherein the cardiac arrhythmia is selected from the group consisting of atrial flutter, atrial arrhythmia and supraventricular tachycardia.

5 12. A method of preventing a condition in a mammal, the prevention of which is effected or facilitated by Kv1.5 inhibition, which comprises administering a compound of Claim 1 in an amount that is effective at inhibiting Kv1.5.

10 13. A method of Claim 12, wherein the condition is cardiac arrhythmia.

14. A method of Claim 13, wherein the cardiac arrhythmia is atrial fibrillation.

15 15. A method of Claim 13, wherein the cardiac arrhythmia is selected from the group consisting of atrial flutter, atrial arrhythmia and supraventricular tachycardia.

16. A method of Claim 12, wherein the condition is a thromboembolic event.

17. A method of Claim 16, wherein the thromboembolic event is a stroke.

20 18. A method of Claim 12, wherein the condition is congestive heart failure.

19. A pharmaceutical formulation comprising a pharmaceutically acceptable carrier and the compound Claim 1 or a pharmaceutically acceptable crystal form or hydrate thereof.

25 20. A pharmaceutical composition made by combining the compound of Claim 1 and a pharmaceutically acceptable carrier.

30 21. A method of treating cardiac arrhythmia comprising administering a compound of Claim 1 with a compound selected from one of the classes of compounds consisting of antiarrhythmic agents having Kv1.5 blocking activities, ACE inhibitors, angiotensin II antagonists, cardiac glycosides, L-type calcium channel blockers, T-type calcium channel blockers, selective and nonselective beta blockers, endothelin antagonists, thrombin inhibitors, aspirin, nonselective NSAIDs, warfarin, factor Xa inhibitors, low molecular weight heparin, unfractionated heparin, clopidogrel, ticlopidine, IIb/IIIa receptor antagonists, 5HT

receptor antagonists, integrin receptor antagonists, thromboxane receptor antagonists, TAFI inhibitors and P2T receptor antagonists.

22. A method for inducing a condition of normal sinus rhythm in a patient  
5 having atrial fibrillation, which comprises treating the patient with a compound of Claim 1.

23. A method for treating tachycardia in a patient which comprises treating the patient with an antitachycardia device in combination with a compound of Claim 1.